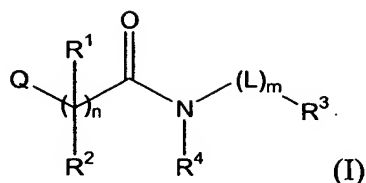


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# Claims

1. A compound having the formula



the *N*-oxide forms, the pharmaceutically acceptable addition salts and the stereochemically isomeric forms thereof, wherein

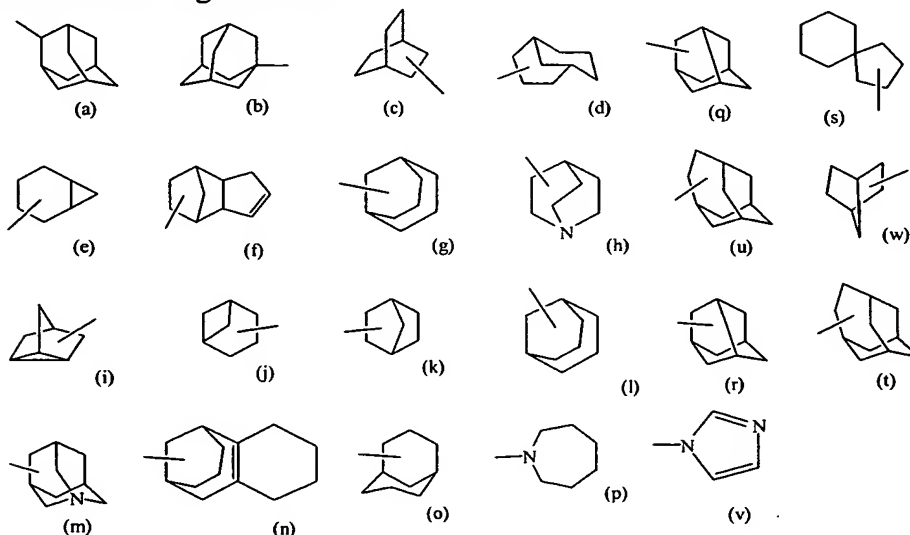
10  $n$  represents an integer being 0, 1 or 2;

$m$  represents an integer being 0 or 1;

$\text{R}^1$  and  $\text{R}^2$  each independently represents hydrogen,  $\text{C}_{1-4}$ alkyl,  $\text{NR}^9\text{R}^{10}$ ,  $\text{C}_{1-4}$ alkyloxy,  $\text{Het}^3\text{-O-C}_{1-4}$ alkyl; or

15  $\text{R}^1$  and  $\text{R}^2$  taken together with the carbon atom with which they are attached form a carbonyl, or a  $\text{C}_{3-6}$ cycloalkyl; and where  $n$  is 2, either  $\text{R}^1$  or  $\text{R}^2$  may be absent to form an unsaturated bond;

$\text{R}^3$  represents hydrogen,  $\text{Ar}^1$ ,  $\text{C}_{1-8}$ alkyl,  $\text{C}_{6-12}$ cycloalkyl or a monovalent radical having one of the following formulae



20 wherein said  $\text{Ar}^1$ ,  $\text{C}_{6-12}$ cycloalkyl or monovalent radical may optionally be substituted with one, or where possible two or three substituents selected from the

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group consisting of C<sub>1-4</sub>alkyl, C<sub>1-4</sub>alkyloxy, phenyl, halo, oxo, carbonyl, 1,3-dioxolyl or hydroxy;

R<sup>4</sup> represents hydrogen, C<sub>1-4</sub>alkyl, or C<sub>2-4</sub>alkenyl;

Q represents C<sub>3-8</sub>cycloalkyl, Het<sup>1</sup> or Ar<sup>2</sup>, wherein said C<sub>3-8</sub>cycloalkyl, Het<sup>1</sup> or Ar<sup>2</sup> are

5 optionally substituted with one or where possible more substituents selected from halo, C<sub>1-4</sub>alkyl, C<sub>1-4</sub>alkyloxy, hydroxy, nitro, Het<sup>4</sup>, phenyl, phenyloxy, C<sub>1-4</sub>alkyloxycarbonyl, hydroxycarbonyl, NR<sup>5</sup>R<sup>6</sup>, C<sub>1-4</sub>alkyloxy substituted with one or where possible two or three substituents each independently selected from C<sub>1-4</sub>alkyl, hydroxycarbonyl, Het<sup>2</sup>, C<sub>1-4</sub>alkyl or NR<sup>7</sup>R<sup>8</sup>,

10 C<sub>2-4</sub>alkenyl substituted with one substituent selected from phenyl-C<sub>1-4</sub>alkyloxycarbonyl, C<sub>1-4</sub>alkyloxycarbonyl, hydroxycarbonyl or Het<sup>5</sup>-carbonyl, and C<sub>1-4</sub>alkyl substituted with one or where possible two or three substituents independently selected from halo, dimethylamine, trimethylamine, amine, cyano, Het<sup>6</sup>, Het<sup>7</sup>-carbonyl, C<sub>1-4</sub>alkyloxycarbonyl or hydroxycarbonyl;

15 R<sup>5</sup> and R<sup>6</sup> are each independently selected from hydrogen, C<sub>1-4</sub>alkyl, C<sub>1-4</sub>alkyloxy-C<sub>1-4</sub>alkyl, C<sub>1-4</sub>alkyloxycarbonyl, C<sub>1-4</sub>alkylcarbonyl, C<sub>1-4</sub>alkylcarbonyl substituted with one or where possible two or three substituents each independently selected from halo, C<sub>1-4</sub>alkyl, and C<sub>1-4</sub>alkyloxy or R<sup>5</sup> and R<sup>6</sup> each independently represent C<sub>1-4</sub>alkyl substituted with phenyl;

20 R<sup>7</sup> and R<sup>8</sup> are each independently selected from hydrogen or C<sub>1-4</sub>alkyl;

R<sup>9</sup> and R<sup>10</sup> are each independently selected from hydrogen, C<sub>1-4</sub>alkyl or C<sub>1-4</sub>alkyloxycarbonyl;

L represents C<sub>1-4</sub>alkyl optionally substituted with one or where possible more substituents selected from C<sub>1-4</sub>alkyl or phenyl;

25 Het<sup>1</sup> represents a heterocycle selected from pyridinyl, piperidinyl, pyrimidinyl, pyrazinyl, piperazinyl, pyridazinyl, indolyl, isoindolyl, indolinyl, furanyl, benzofuranyl, thiazolyl, oxazolyl, isoxazolyl, isothiazolyl, benzothiophenyl, thiophenyl, 1,8-naphthyridinyl, 1,6-naphthyridinyl, quinolinyl, 1,2,3,4-tetrahydro-quinolinyl, isoquinolinyl, 1,2,3,4-tetrahydro-isoquinolinyl, quinoxalinyl, 30 quinazolinyl, phthalazinyl, 2H-benzopyranyl, 3,4-dihydro-2H-benzopyranyl, 2H-benzothiopyranyl, 3,4-dihydro-2H-benzothiopyranyl or 1,3-benzodioxolyl;

35 Het<sup>2</sup> represents a monocyclic heterocycle selected from piperidinyl, pyridinyl, pyridazinyl, pyrimidinyl, pyrazinyl, piperazinyl, 2H-pyrrolyl, pyrrolyl, 2-pyrrolinyl, 3-pyrrolinyl, pyrrolidinyl, or morpholinyl, said Het<sup>2</sup> optionally being substituted with one or where possible two or more substituents each independently selected from hydroxy, C<sub>1-4</sub>alkyl or C<sub>1-4</sub>alkyloxy;

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Het<sup>3</sup> represents a monocyclic heterocycle selected from 2H-pyranyl, 4H-pyranyl, furanyl, tetrahydro-2H-pyranyl, pyridinyl, piperidinyl, or furanyl;

Het<sup>4</sup> represents a monocyclic heterocycle selected from pyridazinyl, pyrimidinyl, pyrrolidinyl, pyrazinyl, piperazinyl, triazolyl, tetrazolyl or morpholinyl, said Het<sup>4</sup> optionally being substituted with one or where possible two or more substituents each independently selected from hydroxy, carbonyl, C<sub>1-4</sub>alkyl or C<sub>1-4</sub>alkyloxy;

Het<sup>5</sup> represents a monocyclic heterocycle selected from pyridazinyl, pyrimidinyl, pyrrolidinyl, pyrazinyl, piperazinyl or morpholinyl, said Het<sup>5</sup> optionally being substituted with one or where possible two or more substituents each independently selected from hydroxy, carbonyl, C<sub>1-4</sub>alkyl or C<sub>1-4</sub>alkyloxy; in particular piperazinyl or morpholinyl;

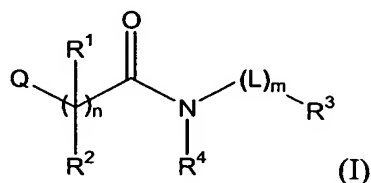
Het<sup>6</sup> represents a monocyclic heterocycle selected from pyridazinyl, pyrimidinyl, pyrrolidinyl, pyrazinyl, piperazinyl or morpholinyl, said Het<sup>6</sup> optionally being substituted with one or where possible two or more substituents each independently selected from hydroxy, carbonyl, C<sub>1-4</sub>alkyl or C<sub>1-4</sub>alkyloxy;

Het<sup>7</sup> represents a monocyclic heterocycle selected from pyridazinyl, pyrimidinyl, pyrrolidinyl, pyrazinyl, piperazinyl or morpholinyl, said Het<sup>7</sup> optionally being substituted with one or where possible two or more substituents each independently selected from hydroxy, carbonyl, C<sub>1-4</sub>alkyl or C<sub>1-4</sub>alkyloxy; in particular selected piperazinyl or morpholinyl;

Ar<sup>1</sup> represents carbocyclic radicals containing one or more rings selected from the group consisting of phenyl, biphenyl, indenyl, 2,3-dihydroindenyl, fluorenyl, 5,6,7,8-tetrahydronaphthyl or naphthyl

Ar<sup>2</sup> represents carbocyclic radicals containing one or more rings selected from the group consisting of phenyl, biphenyl, benzocyclobutenyl, benzocycloheptanyl, benzosubereryl, indenyl, 2,3-dihydroindenyl, fluorenyl, 1,2-dihydronaphthyl, 5,6,7,8-tetrahydronaphthyl or naphthyl.

2. A compound having the formula



the *N*-oxide forms, the pharmaceutically acceptable addition salts and the stereochemically isomeric forms thereof, wherein

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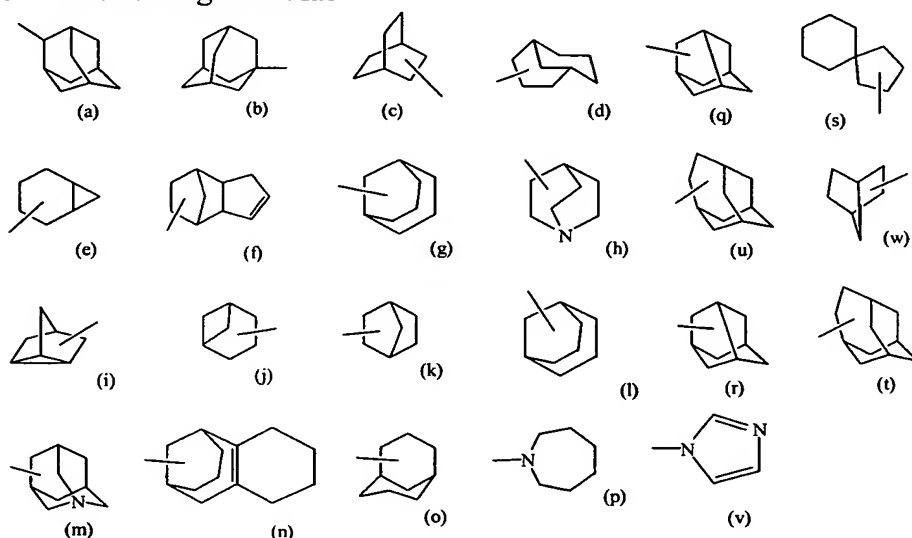
n represents an integer being 0, 1 or 2;

m represents an integer being 0 or 1;

R<sup>1</sup> and R<sup>2</sup> each independently represents hydrogen, C<sub>1-4</sub>alkyl, NR<sup>9</sup>R<sup>10</sup>, C<sub>1-4</sub>alkyloxy,  
5     Het<sup>3</sup>-O-C<sub>1-4</sub>alkyl; or

R<sup>1</sup> and R<sup>2</sup> taken together with the carbon atom with which they are attached form a  
carbonyl, or a C<sub>3-6</sub>cycloalkyl; and where n is 2, either R<sup>1</sup> or R<sup>2</sup> may be absent to  
form an unsaturated bond;

10     R<sup>3</sup> represents hydrogen, Ar<sup>1</sup>, C<sub>1-8</sub>alkyl, C<sub>6-12</sub>cycloalkyl or a monovalent radical having  
one of the following formulae



15     wherein said Ar<sup>1</sup>, C<sub>6-12</sub>cycloalkyl or monovalent radical may optionally be  
substituted with one, or where possible two or three substituents selected from the  
group consisting of C<sub>1-4</sub>alkyl, C<sub>1-4</sub>alkyloxy, phenyl, halo, oxo, carbonyl, 1,3-  
dioxolyl or hydroxy;

R<sup>4</sup> represents hydrogen or C<sub>1-4</sub>alkyl;

20     Q represents C<sub>3-8</sub>cycloalkyl, Het<sup>1</sup> or Ar<sup>2</sup>, wherein said C<sub>3-8</sub>cycloalkyl, Het<sup>1</sup> or Ar<sup>2</sup> are  
optionally substituted with one or where possible more substituents selected from  
halo, C<sub>1-4</sub>alkyl, C<sub>1-4</sub>alkyloxy, hydroxy, nitro, Het<sup>4</sup>, phenyl, phenyloxy, C<sub>1-4</sub>  
alkyloxycarbonyl, hydroxycarbonyl, NR<sup>5</sup>R<sup>6</sup>, C<sub>1-4</sub>alkyloxy substituted with one or  
where possible two or three substituents each independently selected from  
hydroxycarbonyl, Het<sup>2</sup> and NR<sup>7</sup>R<sup>8</sup>, and

C<sub>1-4</sub>alkyl substituted with one or where possible two or three halo substituents;

25     R<sup>5</sup> and R<sup>6</sup> are each independently selected from hydrogen, C<sub>1-4</sub>alkyl, C<sub>1-4</sub>alkyloxyC<sub>1-4</sub>  
alkyl, C<sub>1-4</sub>alkyloxycarbonyl, C<sub>1-4</sub>alkylcarbonyl, C<sub>1-4</sub>alkylcarbonyl substituted with

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one or where possible two or three substituents each independently selected from halo, C<sub>1-4</sub>alkyl, and C<sub>1-4</sub>alkyloxy or R<sup>5</sup> and R<sup>6</sup> each independently represent C<sub>1-4</sub>alkyl substituted with phenyl;

R<sup>7</sup> and R<sup>8</sup> are each independently selected from hydrogen or C<sub>1-4</sub>alkyl;

5 R<sup>9</sup> and R<sup>10</sup> are each independently selected from hydrogen, C<sub>1-4</sub>alkyl or C<sub>1-4</sub>alkyloxycarbonyl;

L represents C<sub>1-4</sub>alkyl optionally substituted with one or where possible more substituents selected from C<sub>1-4</sub>alkyl or phenyl;

10 Het<sup>1</sup> represents a heterocycle selected from pyridinyl, piperidinyl, pyrimidinyl, pyrazinyl, piperazinyl, pyridazinyl, indolyl, isoindolyl, indolinyl, furanyl, benzofuranyl, thiazolyl, oxazolyl, isoxazolyl, isothiazolyl, benzothiophenyl, thiophenyl, 1,8-naphthyridinyl, 1,6-naphthyridinyl, quinolinyl, isoquinolinyl, quinoxalinyl, quinazolinyl, phthalazinyl, or 1,3-benzodioxolyl.;

15 Het<sup>2</sup> represents a monocyclic heterocycle selected from piperidinyl, pyridinyl, pyridazinyl, pyrimidinyl, pyrazinyl, piperazinyl, 2H-pyrrolyl, pyrrolyl, 2-pyrrolinyl, 3-pyrrolinyl, pyrrolidinyl, or morpholinyl;

Het<sup>3</sup> represents a monocyclic heterocycle selected from 2H-pyranyl, 4H-pyranyl, furanyl, tetrahydro-2H-pyranyl, pyridinyl, piperidinyl, or furanyl;

20 Het<sup>4</sup> represents a monocyclic heterocycle selected from pyridazinyl, pyrimidinyl, pyrrolidinyl, pyrazinyl, piperazinyl or morpholinyl, said Het<sup>4</sup> optionally being substituted with one or where possible two or more substituents each independently selected from hydroxy, carbonyl, C<sub>1-4</sub>alkyl or C<sub>1-4</sub>alkyloxy;

25 Ar<sup>1</sup> represents carbocyclic radicals containing one or more rings selected from the group consisting of phenyl, biphenyl, indenyl, 2,3-dihydroindenyl, fluorenyl, 5,6,7,8-tetrahydronaphtyl or naphtyl

Ar<sup>2</sup> represents carbocyclic radicals containing one or more rings selected from the group consisting of phenyl, biphenyl, indenyl, 2,3-dihydroindenyl, fluorenyl, 5,6,7,8-tetrahydronaphtyl or naphtyl.

30 3. A compound according to claims 1 or 2 wherein;  
n represents an integer being 1 or 2 provided that when n represents 2, Q represents Het<sup>1</sup> or Ar<sup>2</sup>, wherein said Het<sup>1</sup> or Ar<sup>2</sup> are optionally substituted with one or where possible more substituents selected from halo, C<sub>1-4</sub>alkyl, C<sub>1-4</sub>alkyloxy, hydroxy, nitro, Het<sup>4</sup>, phenyl, phenyloxy, hydroxycarbonyl, NR<sup>5</sup>R<sup>6</sup>, C<sub>1-4</sub>alkyloxy substituted  
35 with one or where possible two or three substituents each independently selected from hydroxycarbonyl, Het<sup>2</sup> and NR<sup>7</sup>R<sup>8</sup>, and

C<sub>1-4</sub>alkyl substituted with one or where possible two or three halo substituents

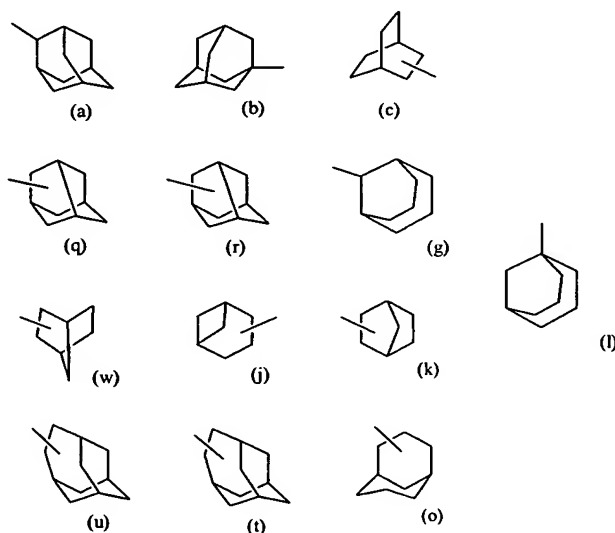
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4. A compound according to any one of claims 1 to 3 wherein;

$R^1$  and  $R^2$  each independently represents hydrogen  $C_{1-4}$ alkyl,  $NR^9R^{10}$ ; or

5  $R^1$  and  $R^2$  taken together with the carbon atom with which they are attached form a  $C_{3-6}$ cycloalkyl; and where n is 2, either  $R^1$  or  $R^2$  may be absent to form an unsaturated bond;

$R^3$  represents a  $C_{6-12}$ cycloalkyl or a monovalent radical having one of the following formulae



10 wherein said  $C_{6-12}$ cycloalkyl or monovalent radical may optionally be substituted with one, or where possible two, three or more substituents selected from the group consisting of  $C_{1-4}$ alkyl,  $C_{1-4}$ alkyloxy, halo, carbonyl, hydroxy, or 1,3-dioxolyl;

15 Q represents  $Het^1$  or  $Ar^2$  wherein said  $Het^1$  or  $Ar^2$  are optionally substituted with one or where possible two or more substituents selected from halo,  $C_{1-4}$ alkyl,  $C_{1-4}$ alkyloxy, hydroxy,  $C_{1-4}$ alkyloxycarbonyl,  $NR^5R^6$ ,  $C_{1-4}$ alkyloxy substituted with one or where possible two or three substituents each independently selected from hydroxycarbonyl,  $Het^2$  and  $NR^7R^8$ , and  $C_{1-4}$ alkyl substituted with one or where possible two or three substituents each independently selected from halo, dimethylamine, amine, cyano,  $Het^6$ ,  $Het^7$ -carbonyl or hydroxycarbonyl;

$R^5$  and  $R^6$  are each independently selected from hydrogen,  $C_{1-4}$ alkyl,  $C_{1-4}$ alkylcarbonyl,  $C_{1-4}$ alkylcarbonyl substituted with one or where possible two or three halo substituents.

25  $R^9$  and  $R^{10}$  are each independently selected from hydrogen or  $C_{1-4}$ alkyl;

L represents a  $C_{1-4}$ alkyl, preferably methyl;

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Het<sup>1</sup> represents a heterocycle selected from pyridinyl, pyrimidinyl, thiophenyl, benzothiophenyl, quinolinyl, 1,2,3,4-tetrahydro-quinolinyl, isoquinolinyl, 1,2,3,4-tetrahydro-isoquinolinyl, 2H-benzopyranyl, 3,4-dihydro-2H-benzopyranyl, 2H-benzothiopyranyl, 3,4-dihydro-2H-benzothiopyranyl or 1,3-benzodioxolyl;

Het<sup>2</sup> represents a monocyclic heterocycle selected from piperidinyl, piperazinyl, pyridinyl, pyrrolidinyl or morpholinyl, said Het<sup>2</sup> optionally being substituted with one or where possible two or more C<sub>1-4</sub>alkyl substituents ;

Het<sup>4</sup> represents tetrazolyl;

Het<sup>5</sup> represents morpholinyl;

Het<sup>6</sup> represents a monocyclic heterocycle selected from pyrrolidinyl, piperazinyl or morpholinyl, said Het<sup>6</sup> optionally being substituted with one or where possible two or more hydroxy substituents, preferably with one hydroxy substituent;

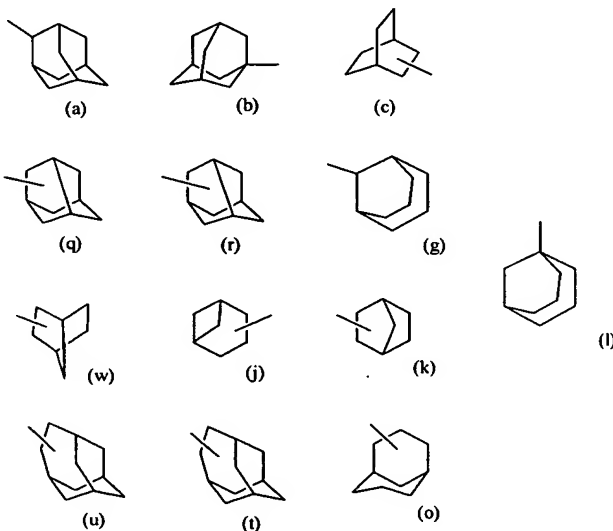
Ar<sup>2</sup> represents carbocyclic radicals containing one or more rings selected from the group consisting of phenyl, benzocyclobutene, benzocycloheptanyl, benzosubereryl, indenyl, 2,3-dihydroindenyl, 5,6,7,8-tetrahydronaphthyl or naphthyl.

5. A compound according to any one of claims 1 to 3 wherein;

R<sup>1</sup> and R<sup>2</sup> each independently represents hydrogen C<sub>1-4</sub>alkyl, NR<sup>9</sup>R<sup>10</sup>; or

R<sup>1</sup> and R<sup>2</sup> taken together with the carbon atom with which they are attached form a C<sub>3-6</sub>cycloalkyl; and where n is 2, either R<sup>1</sup> or R<sup>2</sup> may be absent to form an unsaturated bond;

R<sup>3</sup> represents a C<sub>6-12</sub>cycloalkyl or a monovalent radical having one of the following formulae



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- wherein said C<sub>6-12</sub>cycloalkyl or monovalent radical may optionally be substituted with one, or where possible two, three or more substituents selected from the group consisting of C<sub>1-4</sub>alkyl, C<sub>1-4</sub>alkyloxy, halo, carbonyl, hydroxy, or 1,3-dioxolyl;
- 5 Q represents Het<sup>1</sup> or Ar<sup>2</sup> wherein said Het<sup>1</sup> or Ar<sup>2</sup> are optionally substituted with one or where possible two or more substituents selected from halo, C<sub>1-4</sub>alkyl, C<sub>1-4</sub>alkyloxy, hydroxy, C<sub>1-4</sub>alkyloxycarbonyl, Het<sup>4</sup>, NR<sup>5</sup>R<sup>6</sup>, C<sub>1-4</sub>alkyloxy substituted with one or where possible two or three substituents each independently selected from hydroxycarbonyl, Het<sup>2</sup> and
- 10 NR<sup>7</sup>R<sup>8</sup>, C<sub>2-4</sub>alkenyl substituted with one substituent selected from phenyl-C<sub>1-4</sub>alkyloxycarbonyl or Het<sup>5</sup>-carbonyl and C<sub>1-4</sub>alkyl substituted with one or where possible two or three substituents each independently selected from halo, dimethylamine, amine, cyano, Het<sup>6</sup>,
- 15 Het<sup>7</sup>-carbonyl or hydroxycarbonyl;
- R<sup>5</sup> and R<sup>6</sup> are each independently selected from hydrogen, C<sub>1-4</sub>alkyl, C<sub>1-4</sub>alkylcarbonyl, C<sub>1-4</sub>alkylcarbonyl substituted with one or where possible two or three halo substituents.
- R<sup>9</sup> and R<sup>10</sup> are each independently selected from hydrogen or C<sub>1-4</sub>alkyl;
- 20 L represents a C<sub>1-4</sub>alkyl, preferably methyl;
- Het<sup>1</sup> represents a heterocycle selected from pyridinyl, pyrimidinyl, indolyl, thiophenyl, benzothiophenyl, quinolinyl, 1,2,3,4-tetrahydro-quinolinyl, isoquinolinyl, 1,2,3,4-tetrahydro-isoquinolinyl, 2H-benzopyranyl, 3,4-dihydro-2H-benzopyranyl, 2H-benzothiopyranyl, 3,4-dihydro-
- 25 2H-benzothiopyranyl or 1,3-benzodioxolyl;
- Het<sup>2</sup> represents a monocyclic heterocycle selected from piperidinyl, piperazinyl, pyridinyl, pyrrolidinyl or morpholinyl, said Het<sup>2</sup> optionally being substituted with one or where possible two or more C<sub>1-4</sub>alkyl substituents ;
- Het<sup>4</sup> represents tetrazolyl;
- 30 Het<sup>5</sup> represents morpholinyl;
- Het<sup>6</sup> represents a monocyclic heterocycle selected from pyrrolidinyl, piperazinyl or morpholinyl, said Het<sup>6</sup> optionally being substituted with one or where possible two or more hydroxy substituents, preferably with one hydroxy substituent;
- 35 Het<sup>7</sup> represents a monocyclic heterocycle selected from piperazinyl or morpholinyl, preferably morpholinyl;



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Ar<sup>2</sup> represents carbocyclic radicals containing one or more rings selected from the group consisting of phenyl, benzocyclobutene, benzocycloheptanyl, benzosubereryl, indenyl, 2,3-dihydroindenyl, 5,6,7,8-tetrahydronaphthyl or naphthyl.

5

6. A compound according to any one of claims 1 to 3 wherein;

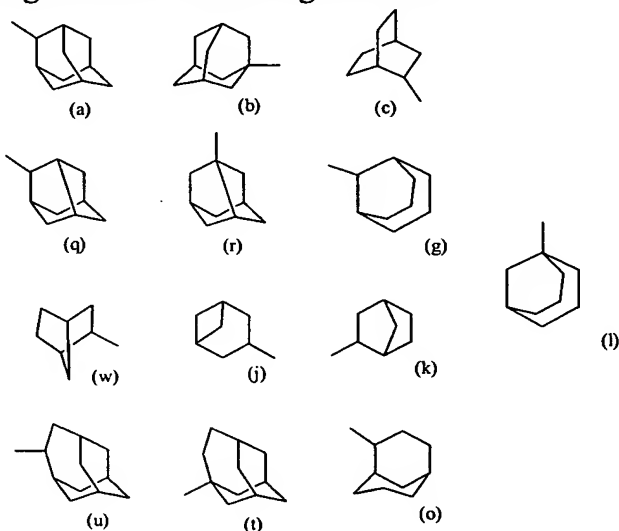
n represents an integer being 0, 1 or 2;

R<sup>1</sup> and R<sup>2</sup> each independently represents hydrogen, C<sub>1-4</sub>alkyl, NR<sup>9</sup>R<sup>10</sup>; or

10

R<sup>1</sup> and R<sup>2</sup> taken together with the carbon atom with which they are attached form a C<sub>3-6</sub>cycloalkyl; and where n is 2, either R<sup>1</sup> or R<sup>2</sup> may be absent to form an unsaturated bond;

R<sup>3</sup> represents a C<sub>6-12</sub>cycloalkyl, preferably cylo-octanyl or a monovalent radical having one of the following formulae



15

, preferably having the formula (a) or (b) above, wherein said C<sub>6-12</sub>cycloalkyl or monovalent radical may optionally be substituted with one, or where possible two, three or more substituents selected from the group consisting of C<sub>1-4</sub>alkyl, C<sub>1-4</sub>alkyloxy, halo or hydroxy;

20

Q represents Het<sup>1</sup> or Ar<sup>2</sup> wherein said Het<sup>1</sup> or Ar<sup>2</sup> are optionally substituted with one or where possible two or more substituents selected from halo, C<sub>1-4</sub>alkyl, C<sub>1-4</sub>alkyloxy, hydroxy, NR<sup>5</sup>R<sup>6</sup>, C<sub>1-4</sub>alkyloxy substituted with one or where possible two, three or more substituents each independently selected from hydroxycarbonyl, Het<sup>2</sup> or NR<sup>7</sup>R<sup>8</sup>,

25

C<sub>2-4</sub>alkenyl substituted with one substituent selected from phenyl-C<sub>1-4</sub>alkyloxy, carbonyl or Het<sup>5</sup>-carbonyl

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and C<sub>1-4</sub>alkyl substituted with one or where possible two or three substituents selected from halo, Het<sup>6</sup>, C<sub>1-4</sub>alkyloxycarbonyl or hydroxycarbonyl;

R<sup>5</sup> and R<sup>6</sup> each independently represent hydrogen or C<sub>1-4</sub>alkyl;

5 R<sup>9</sup> and R<sup>10</sup> each independently represent hydrogen or C<sub>1-4</sub>alkyloxycarbonyl;

L represents C<sub>1-4</sub>alkyl;

Het<sup>1</sup> represents a heterocycle selected from pyridinyl, piperidinyl, thiophenyl, 1,2,3,4-tetrahydro-quinolinyl, 1,2,3,4-tetrahydro-isoquinolinyl, 2H-benzopyranyl, 3,4-dihydro-2H-benzopyranyl, 3,4-dihydro-2H-benzothiopyranyl or 1,3-benzodioxol;

10

Het<sup>2</sup> represents pyridinyl, pyrrolidinyl or morpholinyl;

Het<sup>6</sup> represents morpholinyl;

Ar<sup>2</sup> represents phenyl, benzocyclobutene, benzocycloheptanyl, benzosubereryl, 2,3-dihydroindenyl, 5,6,7,8-tetrahydronaphthyl, naphthyl or indenyl.

15

7. A compound as claimed in claim 1 wherein

n represents an integer being 0, 1 or 2;

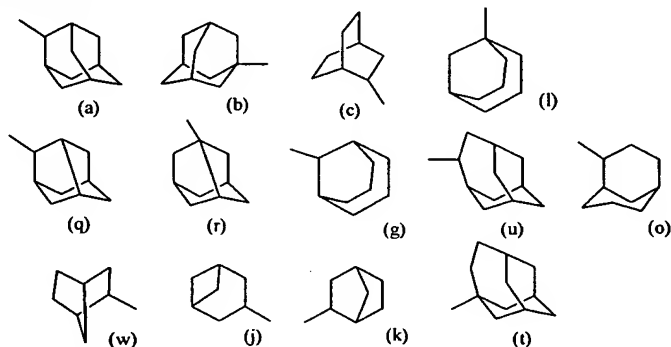
(R<sup>1</sup> and R<sup>2</sup> each independently represents hydrogen C<sub>1-4</sub>alkyl, NR<sup>9</sup>R<sup>10</sup>, C<sub>1-4</sub>alkyloxy; or

20

R<sup>1</sup> and R<sup>2</sup> taken together with the carbon atom with which they are attached form a C<sub>3-6</sub>cycloalkyl; and where n is 2, either R<sup>1</sup> or R<sup>2</sup> may be absent to form an unsaturated bond;

R<sup>3</sup> represents a C<sub>6-12</sub>cycloalkyl, preferably selected from cylo-octanyl and cyclohexyl or R<sup>3</sup> represents a monovalent radical having one of the following formulae

25



, preferably having the formula (a) above, wherein said C<sub>6-12</sub>cycloalkyl or monovalent radical may optionally be substituted with one, or where possible two, three or more substituents selected from the group consisting of C<sub>1-4</sub>alkyl, C<sub>1-4</sub>alkyloxy, halo or hydroxy;

30

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R<sup>4</sup> represents hydrogen or C<sub>1-4</sub>alkyl;

Q represents Het<sup>1</sup> or Ar<sup>2</sup> wherein said C<sub>3-8</sub>cycloalkyl, Het<sup>1</sup> or Ar<sup>2</sup> are optionally substituted with one or where possible two or more substituents selected from halo, C<sub>1-4</sub>alkyl, C<sub>1-4</sub>alkyloxy, hydroxy, nitro, NR<sup>5</sup>R<sup>6</sup>,

5 C<sub>1-4</sub>alkyloxy substituted with one or where possible two, three or more substituents each independently selected from hydroxycarbonyl, Het<sup>2</sup> or NR<sup>7</sup>R<sup>8</sup>,

C<sub>2-4</sub>alkenyl substituted with phenyl-C<sub>1-4</sub>alkyl-oxycarbonyl and C<sub>1-4</sub>alkyl substituted with one or where possible two or three substituents selected from, halo, Het<sup>6</sup>, Het<sup>7</sup>-carbonyl, C<sub>1-4</sub>alkyloxycarbonyl or hydroxycarbonyl;

10 R<sup>5</sup> and R<sup>6</sup> each independently represent hydrogen, C<sub>1-4</sub>alkyl, or C<sub>1-4</sub>alkyl substituted with phenyl;

L represents C<sub>1-4</sub>alkyl;

15 Het<sup>1</sup> represents a heterocycle selected from pyridinyl, thiophenyl, 2H-benzopyranyl, 3,4-dihydro-2H-benzopyranyl, 3,4-dihydro-2H-benzothiopyranyl or 1,3-benzodioxolyl;

Het<sup>2</sup> represents piperidinyl, pyrrolidinyl or morpholinyl;

20 Het<sup>6</sup> represents a monocyclic heterocycle selected from piperazinyl or morpholinyl, preferably morpholinyl;

Ar<sup>2</sup> represents phenyl, benzocyclobutene, benzocycloheptanyl, benzosubereryl, 2,3-dihydroindenyl, 1,2-dihydronaphthyl, 5,6,7,8-tetrahydronaphthyl, naphthyl or indenyl.

- 25 8. A compound as claimed in claim 1 wherein the compound is  
(1 $\alpha$ ,2 $\beta$ ,3 $\beta$ ,5 $\beta$ ,7 $\beta$ )-N-(5-hydroxytricyclo[3.3.1.1<sup>3,7</sup>]dec-2-yl)- $\alpha,\alpha$ -dimethyl-benzeneacetamide;  
(1 $\alpha$ ,2 $\beta$ ,3 $\beta$ ,5 $\beta$ ,7 $\beta$ )-N-(5-hydroxytricyclo[3.3.1.1<sup>3,7</sup>]dec-2-yl)- $\alpha,\alpha$ -dimethyl-3-methyl-benzeneacetamide;  
30 (1 $\alpha$ ,2 $\beta$ ,3 $\beta$ ,5 $\beta$ ,7 $\beta$ )-N-(5-hydroxytricyclo[3.3.1.1<sup>3,7</sup>]dec-2-yl)- $\alpha,\alpha$ -dimethyl-3-methoxy-benzeneacetamide;  
(1 $\alpha$ ,2 $\beta$ ,3 $\beta$ ,5 $\beta$ ,7 $\beta$ )-N-(5-hydroxytricyclo[3.3.1.1<sup>3,7</sup>]dec-2-yl)- $\alpha,\alpha$ -dimethyl-3-hydroxy-benzeneacetamide;  
(1 $\alpha$ ,2 $\beta$ ,3 $\beta$ ,5 $\beta$ ,7 $\beta$ )-N-(5-hydroxytricyclo[3.3.1.1<sup>3,7</sup>]dec-2-yl)- $\alpha,\alpha$ -dimethyl-3,5-dimethyl-benzeneacetamide;  
35 (1 $\alpha$ ,2 $\beta$ ,3 $\beta$ ,5 $\beta$ ,7 $\beta$ )-N-(5-hydroxytricyclo[3.3.1.1<sup>3,7</sup>]dec-2-yl)-3-(phenylmethoxy)benzeneacetamide;

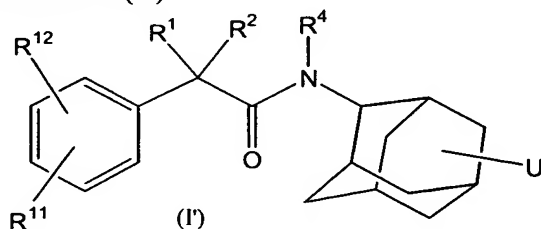
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- (1 $\alpha$ ,2 $\beta$ ,3 $\beta$ ,5 $\beta$ ,7 $\beta$ )-N-(5-hydroxytricyclo[3.3.1.1<sup>3,7</sup>]dec-2-yl)- $\alpha$ , $\alpha$ -dimethyl-3-(carboxymethoxy)-benzeneacetamide;
- (1 $\alpha$ ,2 $\beta$ ,3 $\beta$ ,5 $\beta$ ,7 $\beta$ )-N-(5-hydroxytricyclo[3.3.1.1<sup>3,7</sup>]dec-2-yl)- $\alpha$ , $\alpha$ -dimethyl-3-[2-(4-morpholinyl)ethoxy]-benzeneacetamide;
- 5 (1 $\alpha$ ,2 $\beta$ ,3 $\beta$ ,5 $\beta$ ,7 $\beta$ )-N-(5-fluorotricyclo[3.3.1.1<sup>3,7</sup>]dec-2-yl)- $\alpha$ , $\alpha$ -dimethyl-benzeneacetamide;
- (1 $\alpha$ ,2 $\beta$ ,3 $\beta$ ,5 $\beta$ ,7 $\beta$ )-N-(5-methoxytricyclo[3.3.1.1<sup>3,7</sup>]dec-2-yl)- $\alpha$ , $\alpha$ -dimethyl-benzeneacetamide;
- (1 $\alpha$ ,2 $\alpha$ ,3 $\beta$ ,5 $\beta$ ,7 $\beta$ )-N-(5-methoxytricyclo[3.3.1.1<sup>3,7</sup>]dec-2-yl)- $\alpha$ , $\alpha$ -dimethyl-benzeneacetamide;
- 10 N-(tricyclo[3.3.1.1<sup>3,7</sup>]dec-2-yl)- $\alpha$ , $\alpha$ -dimethyl-benzeneacetamide;
- N-(tricyclo[3.3.1.1<sup>3,7</sup>]dec-2-yl)- $\alpha$ , $\alpha$ -dimethyl-3-(carboxymethoxy)-benzeneacetamide;
- N-(tricyclo[3.3.1.1<sup>3,7</sup>]dec-2-yl)- $\alpha$ , $\alpha$ -dimethyl-3-[2-(4-morpholinyl)ethoxy]-benzeneacetamide;
- 15 N-(tricyclo[3.3.1.1<sup>3,7</sup>]dec-2-yl)- $\alpha$ , $\alpha$ -dimethyl-3,5-dimethoxy-benzeneacetamide;
- N-(tricyclo[3.3.1.1<sup>3,7</sup>]dec-2-yl)- $\alpha$ , $\alpha$ -dimethyl-3-methyl-benzeneacetamide;
- N-(tricyclo[3.3.1.1<sup>3,7</sup>]dec-2-yl)- $\alpha$ , $\alpha$ -dimethyl-3-methoxy-benzeneacetamide;
- 20 N-(tricyclo[3.3.1.1<sup>3,7</sup>]dec-2-yl)- $\alpha$ , $\alpha$ -dimethyl-3-hydroxy-benzeneacetamide;
- N-(tricyclo[3.3.1.1<sup>3,7</sup>]dec-2-yl)- $\alpha$ , $\alpha$ -dimethyl-3,5-dimethyl-benzeneacetamide;
- N-(tricyclo[3.3.1.1<sup>3,7</sup>]dec-2-yl)- $\alpha$ , $\alpha$ -dimethyl-4-fluoro-benzeneacetamide;
- N-(tricyclo[3.3.1.1<sup>3,7</sup>]dec-2-yl)-1-phenyl-cyclopropanecarboxamide;
- N-(tricyclo[3.3.1.1<sup>3,7</sup>]dec-2-yl)- $\alpha$ , $\alpha$ -dimethyl-2,6-difluoro-benzeneacetamide;
- 25 N-(tricyclo[3.3.1.1<sup>3,7</sup>]dec-2-yl)- $\alpha$ , $\alpha$ -dimethyl-2-thiopheneacetamide;
- N-(5-hydroxy-2-adamantyl)-2-methyl-2-(5-methylpyridin-3-yl)propanamide;
- N-(5-hydroxy-2-adamantyl)-2-methyl-2-(6-methylpyridin-2-yl)propanamide;
- 3-(3-{2-[(5-fluoro-2-adamantyl)amino]-1,1-dimethyl-2-oxoethyl}-5-methylphenyl)propanoic acid;
- 30 4-(3-{2-[(5-hydroxy-2-adamantyl)amino]-1,1-dimethyl-2-oxoethyl}-5-methylphenyl)butanoic acid;
- tert*-butyl-4-[3-(3-{2-[(5-hydroxy-2-adamantyl)amino]-1,1-dimethyl-2-oxoethyl}-5-methylphenyl)propanoyl]-1,4-diazepane-1-carboxylate;
- N-(5-hydroxy-2-adamantyl)-5-methoxy-1,2,3,4-tetrahydronaphthalene-1-carboxamide;
- 35 N-2-adamantyl-1,2,3,4-tetrahydroisoquinoline-1-carboxamide;

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N-(5-hydroxy-2-adamantyl)-3,4-dihydroquinoline-1(2*H*)-carboxamide; or a *N*-oxide, a pharmaceutically acceptable addition salt or a stereochemically isomeric form thereof.

- 5 9. A pharmaceutical composition comprising a pharmaceutically acceptable carrier and, as active ingredient, an effective 11 $\beta$ -HSD1 inhibitory amount of a compound as described in any one of claims 1 to 8.
- 10 10. A process of preparing a pharmaceutical composition as defined in claim 8, characterized in that, a pharmaceutically acceptable carrier is intimately mixed with an effective 11 $\beta$ -HSD1 inhibitory amount of a compound as described in any one of claims 1 to 8.
- 15 11. A compound as claimed in any one of claims 1 to 8 for use as a medicine.
12. Use of a compound as claimed in any one of claims 1 to 8 in the manufacture of a medicament for treating pathologies associated with excess cortisol formation such as for example, obesity, diabetes, obesity related cardiovascular diseases, dementia, cognition, osteoporosis and glaucoma.
- 20 13. A compound of formula (I')



the *N*-oxide forms, the pharmaceutically acceptable addition salts and the stereochemically isomeric forms thereof wherein

- 25 R<sup>1</sup> and R<sup>2</sup> each independently represents hydrogen, C<sub>1-4</sub>alkyl, NR<sup>9</sup>R<sup>10</sup>, C<sub>1-4</sub>alkyloxy or Het<sup>3</sup>-O-C<sub>1-4</sub>alkyl; preferably C<sub>1-4</sub>alkyl in particular methyl; or R<sup>1</sup> and R<sup>2</sup> taken together with the carbon atom with which they are attached from a C<sub>3-6</sub>cycloalkyl, in particular cyclopropyl or cyclobutyl;
- 30 R<sup>4</sup> represents hydrogen, C<sub>1-4</sub>alkyl, C<sub>2-4</sub>alkenyl;
- U represents hydrogen, C<sub>1-4</sub>alkyl, C<sub>1-4</sub>alkyloxy, phenyl, halo, oxo, carbonyl or hydroxy
- R<sup>5</sup> and R<sup>6</sup> are each independently selected from hydrogen, C<sub>1-4</sub>alkyl, C<sub>1-4</sub>alkyloxyC<sub>1-4</sub>alkyl, C<sub>1-4</sub>alkyloxycarbonyl, C<sub>1-4</sub>alkylcarbonyl, C<sub>1-4</sub>alkylcarbonyl substituted with

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- one or where possible two or three substituents each independently selected from halo, C<sub>1-4</sub>alkyl, and C<sub>1-4</sub>alkyloxy or R<sup>5</sup> and R<sup>6</sup> each independently represent C<sub>1-4</sub>alkyl substituted with phenyl;
- R<sup>7</sup> and R<sup>8</sup> are each independently selected from hydrogen or C<sub>1-4</sub>alkyl;
- 5 R<sup>9</sup> and R<sup>10</sup> are each independently selected from hydrogen, C<sub>1-4</sub>alkyl or C<sub>1-4</sub>alkyloxycarbonyl;
- R<sup>11</sup> and R<sup>12</sup> are each independently selected from hydrogen, halo, C<sub>1-4</sub>alkyl, C<sub>1-4</sub>alkyloxy, hydroxy, nitro, Het<sup>4</sup>, phenyl, phenyloxy, C<sub>1-4</sub>alkyloxycarbonyl, hydroxycarbonyl, NR<sup>5</sup>R<sup>6</sup>, C<sub>1-4</sub>alkyloxy substituted with one or where possible two or three substituents each independently selected from hydroxycarbonyl, Het<sup>2</sup> and NR<sup>7</sup>R<sup>8</sup>, C<sub>2-4</sub>alkenyl substituted with one substituent selected from phenyl-C<sub>1-4</sub>alkyl-oxycarbonyl, C<sub>1-4</sub>alkyloxycarbonyl, hydroxycarbonyl, Het<sup>5</sup>-carbonyl, and C<sub>1-4</sub>alkyl substituted with one or where possible two or three substituents independently selected from halo, dimethylamine, trimethylamine, amine, cyano, 10 Het<sup>6</sup>, Het<sup>7</sup>-carbonyl, C<sub>1-4</sub>alkyloxycarbonyl or hydroxycarbonyl;
- Het<sup>1</sup> represents a heterocycle selected from pyridinyl, piperidinyl, pyrimidinyl, pyrazinyl, piperazinyl, pyridazinyl, indolyl, isoindolyl, indolinyl, furanyl, benzofuranyl, thiazolyl, oxazolyl, isoxazolyl, isothiazolyl, benzothiophenyl, thiophenyl, 1,8-naphthyridinyl, 1,6-naphthyridinyl, quinolinyl, isoquinolinyl, 1,2,3,4-tetrahydro-isoquinolinyl, quinoxalinyl, quinazolinyl, phthalazinyl, 2H-benzopyranyl, 3,4-dihydro-2H-benzopyranyl, 2H-benzothiopyranyl, 3,4-dihydro-2H-benzothiopyranyl or 1,3-benzodioxolyl.;
- 20 Het<sup>2</sup> represents a monocyclic heterocycle selected from piperidinyl, pyridinyl, pyridazinyl, pyrimidinyl, pyrazinyl, piperazinyl, 2H-pyrrolyl, pyrrolyl, 2H-pyrrolinyl, 3-pyrrolinyl, pyrrolidinyl, or morpholinyl, said Het<sup>2</sup> optionally being substituted with one or where possible two or more substituents each independently selected from hydroxy, carbonyl, C<sub>1-4</sub>alkyl or C<sub>1-4</sub>alkyloxy.;
- 25 Het<sup>3</sup> represents a monocyclic heterocycle selected from 2H-pyranyl, 4H-pyranyl, furanyl, tetrahydro-2H-pyranyl, pyridinyl, piperidinyl, or furanyl;
- 30 Het<sup>4</sup> represents a monocyclic heterocycle selected from pyridazinyl, pyrimidinyl, pyrrolidinyl, pyrazinyl, piperazinyl, triazolyl, tetrazolyl or morpholinyl, said Het<sup>4</sup> optionally being substituted with one or where possible two or more substituents each independently selected from hydroxy, carbonyl, C<sub>1-4</sub>alkyl or C<sub>1-4</sub>alkyloxy;
- 35 Het<sup>5</sup> represents a monocyclic heterocycle selected from pyridazinyl, pyrimidinyl, pyrrolidinyl, pyrazinyl, piperazinyl or morpholinyl, said Het<sup>5</sup> optionally being substituted with one or where possible two or more substituents each

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independently selected from hydroxy, carbonyl, C<sub>1-4</sub>alkyl or C<sub>1-4</sub>alkyloxy;  
preferably piperazinyl or morpholinyl;

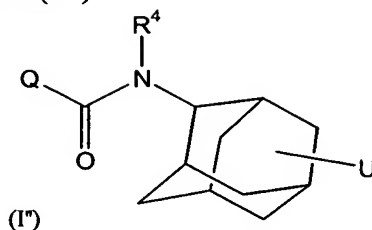
Het<sup>6</sup> represents a monocyclic heterocycle selected from pyridazinyl, pyrimidinyl,  
pyrrolidinyl, pyrazinyl, piperazinyl or morpholinyl, said Het<sup>6</sup> optionally being  
5 substituted with one or where possible two or more substituents each  
independently selected from hydroxy, carbonyl, C<sub>1-4</sub>alkyl or C<sub>1-4</sub>alkyloxy;

Het<sup>7</sup> represents a monocyclic heterocycle selected from pyridazinyl, pyrimidinyl,  
pyrrolidinyl, pyrazinyl, piperazinyl or morpholinyl, said Het<sup>7</sup> optionally being  
substituted with one or where possible two or more substituents each  
10 independently selected from hydroxy, carbonyl, C<sub>1-4</sub>alkyl or C<sub>1-4</sub>alkyloxy;  
preferably piperazinyl or morpholinyl; in particular morpholinyl.



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14. A compound of formula (I'')



the *N*-oxide forms, the pharmaceutically acceptable addition salts and the  
5 stereochemically isomeric forms thereof, wherein

$R^4$  represents hydrogen,  $C_{1-4}$ alkyl,  $C_{2-4}$ alkenyl;

U represents hydrogen,  $C_{1-4}$ alkyl,  $C_{1-4}$ alkyloxy, phenyl, halo, oxo, carbonyl or hydroxy

Q represents  $Het^1$  or  $Ar^2$ , wherein said  $Het^1$  or  $Ar^2$  are optionally substituted with one

10 or where possible more substituents selected from halo,  $C_{1-4}$ alkyl,  $C_{1-4}$ alkyloxy, hydroxy, nitro,  $Het^4$ , phenyl, phenyloxy,  $C_{1-4}$ alkyloxycarbonyl, hydroxycarbonyl,  $NR^5R^6$ ,

$C_{1-4}$ alkyloxy substituted with one or where possible two or three substituents each independently selected from hydroxycarbonyl,  $Het^2$  and  $NR^7R^8$ , and

15  $C_{1-4}$ alkyl substituted with one or where possible two or three substituents independently selected from halo or hydroxycarbonyl;

$R^5$  and  $R^6$  are each independently selected from hydrogen,  $C_{1-4}$ alkyl,  $C_{1-4}$ alkyloxy,  $C_{1-4}$ alkyl,  $C_{1-4}$ alkyloxycarbonyl,  $C_{1-4}$ alkylcarbonyl,  $C_{1-4}$ alkylcarbonyl substituted with one or where possible two or three substituents each independently selected from  
20 halo,  $C_{1-4}$ alkyl, and  $C_{1-4}$ alkyloxy or  $R^5$  and  $R^6$  each independently represent  $C_{1-4}$ alkyl substituted with phenyl;

$R^7$  and  $R^8$  are each independently selected from hydrogen or  $C_{1-4}$ alkyl;

$R^9$  and  $R^{10}$  are each independently selected from hydrogen,  $C_{1-4}$ alkyl or  $C_{1-4}$ alkyloxycarbonyl;

25  $Het^1$  represents a bicyclic heterocycle selected from indolyl, isoindolyl, indolinyl, benzofuranyl, benzothiophenyl, 1,8-naphthyridinyl, 1,6-naphthyridinyl, quinolinyl, 1,2,3,4-tetrahydro-quinolinyl, isoquinolinyl, 1,2,3,4-tetrahydro-isoquinolinyl, quinoxalinyl, quinazolinyl, phthalazinyl, 2H-benzopyranyl, 3,4-dihydro-2H-benzopyranyl, 2H-benzothiopyranyl, 3,4-dihydro-2H-benzothiopyranyl or 1,3-benzodioxolyl.;  
30

$Het^2$  represents a monocyclic heterocycle selected from piperidinyl, pyridinyl, pyridazinyl, pyrimidinyl, pyrazinyl, piperazinyl, 2H-pyrrolyl, pyrrolyl, 2-pyrrolinyl, 3-pyrrolinyl, pyrrolidinyl, or morpholinyl, said  $Het^2$  optionally being



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- substituted with one or where possible two or more substituents each independently selected from hydroxy, C<sub>1-4</sub>alkyl or C<sub>1-4</sub>alkyloxy;
- Het<sup>3</sup> represents a monocyclic heterocycle selected from 2H-pyranyl, 4H-pyranyl, furanyl, tetrahydro-2H-pyranyl, pyridinyl, piperidinyl, or furanyl;
- 5 Het<sup>4</sup> represents a monocyclic heterocycle selected from pyridazinyl, pyrimidinyl, pyrrolidinyl, pyrazinyl, piperazinyl or morpholinyl, said Het<sup>4</sup> optionally being substituted with one or where possible two or more substituents each independently selected from hydroxy, carbonyl, C<sub>1-4</sub>alkyl or C<sub>1-4</sub>alkyloxy;
- 10 Ar<sup>2</sup> represents carbocyclic radicals containing two rings selected from the group consisting of benzocyclobutene, benzocycloheptanyl, benzosurbenyl, indenyl, 2,3-dihydroindenyl, 5,6,7,8-tetrahydronaphthyl or naphthyl.
- 15 15. A compound of formula (I') or (I'') for use as a medicine.
- 15 16. Use of a compound of formula (I') or (I'') in the manufacture of a medicament for treating pathologies associated with excess cortisol formation such as for example, obesity, diabetes, obesity related cardiovascular diseases, dementia, cognition, osteoporosis and glaucoma.
- 20 17. A method to prepare 1-hydroxy-4-aminoadamantane said method comprising
- the reductive amination of the corresponding ketone (XIII);
  - separating the thus obtained stereomers of the amine of formula (XVIII); and
  - debenzylating the compounds of formula (XVIII)

